884-Pos Board B664
Single-Read De Novo Sequencing Using Nanopore Mspa
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Biological nanopores such as MspA are used in a promising next-generation DNA sequencing technique capable of achieving long, single-molecule reads. In our experiments, current is driven through the ~1 nm constriction of the protein nanopore MspA. Single molecules of DNA are pulled in by the voltage, and held in place by a DNA polymerase. The polymerase pulls the DNA under load in single-nucleotide steps. The current depends on the bases in the narrowest part of the pore. De novo sequencing accuracy with this method is limited by the inability to distinguish different base sequences that have the same currents, and by unpredictable deviations from forward-stepping behavior by the polymerase. We show that by driving the current through the pore with a varying voltage, we obtain additional information about the base content of the DNA. Varying the voltage allows for the identification and correction of skipping and backstepping behavior, and can discriminate between nucleotide sequences that are indistinguishable when driving the system at a constant voltage. We provide initial results demonstrating that this method greatly improves single read de novo sequencing fidelity.

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Deconstructing Structural Transitions via Thermal Transport
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Structural transitions appear everywhere: proteins fold, nanotubes collapse, DNA denatures, ice melts, and so on. In biology, these transitions play a role in processes such as transcription and also determine protein function. Yet, at the same time, they give examples of highly nonlinear processes that are challenging to model and understand. I will discuss one such transition - the denaturation of DNA, where its double stranded form unravels into two single strands. There are many models that can describe certain aspects of this transition equally well, such as the fraction of bound base pairs versus temperature. I will show, however, that two well-known models yield drastically different predictions for thermal transport. The latter can then be used to ''peek inside'' DNA and understand what is happening during the denaturation transition. Thus, on the one hand, thermal transport gives a method to probe structural transitions in biological molecules and other materials. On the other hand, molecular systems and materials with nonlinear structural transitions also give opportunities for developing novel thermal devices.

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Quantitative Analysis and Optimization of On-Chip Interference Functionalities for Nanophotonics Standing Wave Array Traps
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The advent of an on-chip optical trapping platform based on nanophotonic interference has allowed parallel processing of biomolecules and holds the promise to make single molecule manipulation and precision measurements more easily and broadly available. The nanophotonic standing wave array trap (nSWAT) device[1] has recently been demonstrated to be capable of trapping an array of beads by the evanescent field of the standing wave of a nanophotonic waveguide. Here, in order to more efficiently utilize the input power, we quantitatively analyze the laser power distribution on-chip, and propose and demonstrate an alternative method to generate on-chip interference for nSWAT. We show that this method improves laser power at the trapping region and thus allows for the generation of increased trapping stiffness. This thus demonstrates a method towards nSWAT optimization.

1. M. Soltani, J. Lin, R.A. Forties, J.T. Inman, S.N. Saraf, R. M. Fulbright, M. Lipson, M. D. Wang 'Nanophotonic trapping for precise manipulation of biomolecular arrays' Nature nanotechnology, 2014

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DNA-Modified Polymer Pores Enable Ph- and Voltage-Gated Control of Channel Flux
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Biological channels embedded in cell membranes regulate ionic transport by responding to external stimuli such as pH, voltage, and molecular binding. Mimicking the gating properties of these biological structures would be instrumental in the preparation of smart membranes used in biosensing, drug delivery, and ionic circuit construction. Here we present a new concept for building synthetic nanopores that can simultaneously respond to pH and transmembrane potential changes. These pores allow for the complete switching off of the channel flux as well as the ability to tune the preferred direction of ion current flow. DNA oligomers containing protonatable A and C bases are attached at the narrow opening of an asymmetrical track etched polymer nanopore. Lowering the pH to 5.5 causes the positively charged DNA molecules to bind to the negative backbone of other nearby strands. This creates an electrostatic mesh that closes the pore to unprecedentedly high resistances of several tens of gigaohms. In contrast, pores modified with DNA oligomers containing G and T bases did not show strong pH sensitivity. At neutral pH values, voltage switching causes the isolated DNA strands to undergo nanomechanical movement, as seen by a reversible current modulation. We provide evidence that the pH-dependent reversible closing mechanism is robust and applicable for nanopores with opening diameters of up to 14 nm. The concept of creating an electrostatic mesh should not be unique to DNA and may be applied to different organic polymers.

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Building Connections Between Terminals with Location Uncertainty Using DNA Nanotubes
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While DNA nanostructures designed with 2- and 3-dimensional nanoscale attributes can now be routinely synthesized, we cannot yet assemble structures whose dimensions depend on the particularities of its environment. For example, an important assembly problem of this type is the construction of a wire or tether that connects two terminals when the location of (or distance between) the terminals is unknown or uncertain. Fabricating such assembly by top down methods is challenging as it is not a parallel process and nanometer scale positioning accuracy is required. We propose to develop a bottom-up method for interconnect assembly where chemical tags located at terminals guide interconnect self-assembly.
DNA nanotubes, which are 20 nm in diameter and self-assembled from small DNA tiles, are used as connection filaments. We design and construct DNA origami seeds that serve as nanotube nucleation templates to control DNA nanotube assembly. The idea is that by placing DNA origami seeds at the two terminals, two DNA nanotubes would nucleate from the respective seeds, grow longer (by addition of DNA tiles to their growing ends), diffuse until the two growing ends find each other and join to form a continuous single DNA nanotube.
We successfully demonstrate that when these seeds are randomly deposited and affixed to passivized glass surfaces, DNA nanotubes grown from these points join together to create point-to-point interconnects with lengths varying from 100 nm up to 10 microns. This autonomous assembly process could potentially be used to connect nanodevices that are either randomly arrayed on a surface or are positioned using low-resolution lithography, and techniques to functionalize DNA could conceivably allow us to construct optical or electronic links between these devices using the DNA nanotube filaments as a scaffold.